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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Dean Pettit and Claudia M. Jochheim
Application No.	:	09/800,016
Filed	:	March 5, 2001
For	:	USE OF EDTA IN STABILIZING GRANULOCYTE MACROPHAGE COLONY-STIMULATING FACTOR (As Amended)

Examiner	:	Lorraine Spector, Ph.D.
Art Unit	:	1647
Docket No.	:	140145.410
Date	:	June 27, 2006

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

I, Catherine Scholz, declare:

1. I am a Senior Clinical Research Scientist at Berlex, Inc. (a U.S. subsidiary of Schering AG, the assignee of the present application), and my curriculum vitae is attached as Exhibit 1.

2. I have reviewed the Office Action dated October 27, 2005, in the subject application, including the rejections under 35 U.S.C. 103(a), and provide this Declaration to assist the Examiner in evaluating the non-obviousness of the claimed subject matter of the application.

3. The studies presented herein were performed by me, by those under my direct supervision, or are within my personal knowledge.

4. Methods and Materials: Two Phase I studies were performed to evaluate single dose pharmacokinetics of a liquid formulation of sargramostim with EDTA at various doses. Additionally, in the second study, the pharmacokinetic profile of the liquid formulation of sargramostim with EDTA was compared with that of a lyophilized formulation of sargramostim without EDTA.

In both studies, the liquid formulation of sargramostim with EDTA (also referred to as "sargramostim EDTA") was supplied as vials containing 500 μg (2.8×10^6 IU/ml) sargramostim, 1.9 mg/ml EDTA, USP, and 1.15% benzyl alcohol, NF, in a 1 ml solution. Each vial also contained 40 mg/ml mannitol, USP; 10 mg/ml sucrose, NF; and 1.2 mg/ml Tris (tromethamine), USP, as excipients. In the second study, lyophilized sargramostim (also referred to "sargramostim LY") was supplied as a lyophilized powder in vials containing 500 μg of sargramostim. In addition, each vial contained 40 mg mannitol, USP; 10 mg sucrose, NF; and 1.2 mg Tris (tromethamine), USP. Lyophilized sargramostim was reconstituted by trained personnel by injecting 1.0 ml of bacteriostatic water for injection (BWI), USP, containing 0.9% benzyl alcohol, into each vial.

The first study was a Phase I randomized, crossover study with three sargramostim dose levels, two treatment groups (Japanese and Caucasian) and six treatment sequences. Each subject was to receive a total of two single subcutaneous doses of liquid sargramostim with EDTA, with a washout period of at least 14 days between each dose. Three different sargramostim dose levels (2, 6, and 8 μg/kg) were evaluated for each ethnicity. A total of 34 blood samples were to be collected for pharmacokinetic analysis on Days 1-2 and 15-16.

The second study, a Phase 1 randomized two-part crossover study, was performed to evaluate the bioavailability of the two above-described formulations of sargramostim in healthy male subjects: sargramostim EDTA (sargramostim with EDTA, subcutaneous injection, SC) and sargramostim LY (reconstitutued lyophilized sargramostim, SC). Part 1 was a double-blind, placebo-controlled, three-way crossover substudy with three single-dose study drug treatments administered consecutively over

three respective time periods. Study drug treatment consisted of a single 6 µg/kg SC dose of sargramostim EDTA, sargramostim LY, and placebo EDTA administered consecutively to each subject in accordance with the assigned treatment sequence. Following receipt of the initial dose of study drug, each subject underwent a minimum study drug washout period of 14 days prior to receiving the next dose of study drug. Part 2 was an open-label two-way crossover substudy with two single-dose study drug treatments administered consecutively over two time periods. Study drug treatment consisted of single 500 µg SC and IV doses of sargramostim EDTA administered consecutively to each subject in accordance with the assigned treatment sequence. Following administration of the initial dose of study drug, each subject underwent a minimum study drug washout period of 14 days prior to receiving the next dose of study drug. The IV dose was administered as a 2-hour infusion. A total of 51 blood samples were to be collected for pharmacokinetic analysis on Days 1-2, 15-16 and 29-30.

Serum samples from both studies were analyzed for sargramostim concentration using a validated ELISA method. Briefly, the method consisted of a "sandwich" ELISA assay design based on the R&D Systems high-sensitivity GM-CSF ELISA immunoassay. Murine monoclonal antibodies specific for GM-CSF were employed for both the immobilized antibody and the conjugated antibody. The absorbance of the enzyme substrate reaction was measured at 490-650 nm. The intensity of the color produced (absorbance) was directly proportional to the concentration of sargramostim present. The lower and upper limits of quantification were 2.17 pg/ml and 93.4 pg/ml, respectively.

Serum concentration-time profiles of individual subjects were analyzed using a compartment model independent (CMID) method employing a validated computer program WINNOLIN® Professional version 4.1a (Pharsight Corp.) running on a personal computer (Pentium 4, 1.8 GHz, Microsoft Windows XP, Professional Version 2002, service pack 2).

Subcutaneous administration: WINNOLIN® Professional (Version 4.1a) Model 200 (extravascular input) was used for the CMID method.

The maximum serum concentration (Cmax) and time to maximum concentration (tmax) were the observed maximum values from the tabulated data. The area under the serum concentration-time curve from 0 to tlast [AUC(0-tlast), where tlast was the time of the last quantifiable sample] was calculated using the trapezoidal rule (linear up/log down). The AUC(0-tlast) was extrapolated to infinity (inf) to give AUC [AUC= AUC(0-tlast) + AUC(tlast-inf)]. AUC (tlast-inf) was computed as AUC(tlast-inf) = concentration at tlast (Ctlast/λz), where λz was the first-order rate constant describing the terminal disposition phase and Ctlast was the observed sargramostim concentration in serum at tlast. The λz was obtained from the slope of the least-squares regression (with uniform weighting) of the natural logarithm of the terminal-phase drug concentration values over time. The algorithm used by WINNOLIN® was as follows: Regressions were repeated using the last three data points with non-zero concentrations, then the last four data points, *etc.* The regression with the largest R^2 was selected to estimate λz. If the adjusted R^2 did not improve but was within 0.0001 of the largest R^2 value, the regression with the largest number of points was used. The half-life of the terminal disposition phase was computed as terminal $t_{1/2}$ = ln 2/λz. The λz was computed by WinNonlin using the above described methodology unless manual interpretation was necessary to select the optimal time points to represent the terminal disposition phase.

The apparent total clearance (CL/f) was calculated as CL/f = D/AUCinf, where D was the dose of sargramostim in micrograms. The apparent volume of distribution during the terminal disposition phase was calculated as Vz/f = (CL/f)/λz. Mean residence time (MRT) after SC administration (0-inf) was calculated as MRT = AUMC/AUC. Area under the first moment curve from 0 to tlast, AUMC(0-tlast), was calculated using the linear trapezoidal rule. The AUMC(0-tlast) was extrapolated to infinity to give the total AUMC [AUMC = AUMC(0-tlast) + AUMC(tlast-inf)]. The AUMC(tlast-inf) was computed as: AUMC(tlast-inf) = Ctlast/λz^2 + tlast x Ctlast/ λz.

Intravenous Infusion: WINNOLIN® Professional (Version 4.1a) Model 202 (constant infusion input) was used for the CMID method. The maximum serum concentration (Cmax) and time to maximum concentration (tmax) were the observed

maximum values from the tabulated data. The area under the serum concentration-time curve from 0 to tlast [AUC(0-tlast), where tlast was the time of the last quantifiable sample] was calculated using the trapezoidal rule (linear/log trapezoidal). The AUC(0-tlast) was extrapolated to infinity (inf) to give AUC [AUC= AUC(0-tlast) + AUC(tlast-inf)]. AUC (tlast-inf) was computed as AUC(tlast-inf) = concentration at tlast (Ctlast/λz), where λz was the first-order rate constant describing the terminal disposition phase and Ctlast was the observed sargramostim concentration in serum at tlast. The λz was obtained from the slope of the least-squares regression (with uniform weighting) of the natural logarithm of the terminal-phase drug concentration values over time. The algorithm used by WinNonlin was as follows: Regressions were repeated using the last three data points with non-zero concentrations, then the last four data points, etc. The regression with the largest R^2 was selected to estimate λz. If the adjusted R^2 did not improve but was within 0.0001 of the largest R^2 value, the regression with the largest number of points was used. The half-life of the terminal disposition phase was computed as terminal $t_{1/2}$ = ln 2/λz. The λz was computed by WinNonlin using the above described methodology unless manual interpretation was necessary to select the optimal time points to represent the terminal disposition phase.

The total clearance (CL) was calculated as CL = D/AUCinf, where D was the dose of sargramostim in micrograms. The volume of distribution during the terminal disposition phase was calculated as Vz = (CL)/λz. Mean residence time (MRT) after IV administration (0-inf) was calculated as MRT = [AUMC/AUC]-Ro/2, where Ro is the length of the infusion. Area under the first moment curve from 0 to tlast, AUMC(0-tlast), was calculated using the linear trapezoidal rule. The AUMC(0-tlast) was extrapolated to infinity to give the total AUMC [AUMC = AUMC(0-tlast) + AUMC(tlast-inf)]. The AUMC(tlast-inf) was computed as: AUMC(tlast-inf) = Ctlast/λz^2 + tlast x Ctlast/ λz.

5. Results: The GM-CSF formulation with EDTA showed a unique pharmacokinetic profile consisting of a two-peak absorption profile and a decreased time to maximum serum concentration (*see*, Exhibits 2, 3, 4, 5, and 6). More specifically, after a single SC dose of sargramostim EDTA, the sargramostim

concentration-time curve demonstrated a double-peak absorption profile. During the initial absorption phase, sargramostim concentrations rapidly increased, reaching peak serum concentration at 0.25 hour post injection. This was followed by a slower absorption phase where maximum sargramostim serum concentration (Cmax) was achieved at 2.5 hours post injection. The mean (geometric) Cmax after subcutaneous administration of 6 µg/kg ranged from 3.06 to 5.24 ng/ml. The slower absorption phase allowed for sustained detectable levels throughout 12 to 24 hours post administration. In contrast, sargramostim LY demonstrated only the single, slower absorption process, reaching a mean (geometric) Cmax of 2.96 ng/ml at 4 hours post injection.

This initial extremely rapid diffusion of sargramostim into the systemic circulation (time to peak concentration 0.25 hours) after subcutaneous administration of sargramostim EDTA, although similar to that observed after intravenous (i.v.) infusion administration of GM-CSF at a rate of 4.2 µg/min during the first 30 minutes of the infusion (*see*, Exhibit 6), was unique and not characteristic of products given by the subcutaneous route of administration. The rate of delivery of sargramostim into systemic circulation was greatly enhanced by the liquid formulation containing EDTA because it was not evident following subcutaneous administration of the lyophilized formulation (*i.e.*, the GM-CSF formulation without EDTA), which demonstrates a single, slower absorption profile (*see*, Exhibits 2 and 3). The complex absorption associated with the GM-CSF formulation containing EDTA did not appear to be dose dependent, nor influenced by ethnicity, as evidenced in the first study (*see*, Exhibits 4 and 5).

The pharmacokinetic differences between the GM-CSF formulations with EDTA and without EDTA did not appear to result from different degradation rates of GM-CSF in the two formulations. In general, the observed PK differences between the formulations were limited to the initial rate of absorption. No apparent differences were seen in the distribution or elimination PK profile. In the second study, the mean (SD) terminal half-life of sargramostim after SC administration was 1.74 (0.47) h for EDTA and 1.39 (0.36) h for LY (*see*, Exhibits 2 and 3).

The mean PK parameters by treatment from both studies are summarized in Tables 1 and 2 below.

Table 1: First Study—sargramostim PK parameters following single SC administration

Parameter	Japanese			Caucasian		
	2 µg/kg n = 20	6 µg/kg n = 19	8 µg/kg n = 19	2 µg/kg n = 19	6 µg/kg n = 18	8 µg/kg n = 19
Cmax (ng/mL)						
Arithmetic mean ± SD	1.89 ± 0.70	5.52 ± 1.85	7.20 ± 1.53	1.62 ± 0.73	4.61 ± 1.64	6.48 ± 2.06
Geometric mean (%CV)	1.77 (48.8)	5.24 (39.8)	7.05 (23.3)	1.50 (47.4)	4.32 (46.1)	6.17 (38.0)
Minimum-maximum	0.73 - 3.51	2.55 - 9.11	5.12 - 10.6	0.87 - 3.72	2.12 - 7.74	3.77 - 10.2
AUC (ng*h/mL)						
Arithmetic mean ± SD	5.37 ± 2.56	24.0 ± 6.15	31.8 ± 5.11	4.71 ± 2.89	20.8 ± 6.96	33.5 ± 7.92
Geometric mean (%CV)	4.99 (44.5)	23.2 (31.7)	31.4 (18.7)	4.18 (62.0)	19.5 (50.2)	32.6 (26.5)
Minimum-maximum	2.28 - 15.2	12.4 - 36.1	21.2 - 41.2	1.25 - 15.5	5.45 - 38.0	21.0 - 49.7
tmax (h)						
Arithmetic mean ± SD	0.73 ± 1.06	0.83 ± 1.01	0.77 ± 0.92	0.39 ± 0.43	0.44 ± 0.66	0.98 ± 1.48
Median	0.25	0.25	0.25	0.25	0.25	0.25
Minimum-maximum	0.25 - 4.00	0.25 - 3.00	0.25 - 3.02	0.25 - 2.00	0.25 - 3.07	0.25 - 5.00
t1/2 (h)						
Arithmetic mean ± SD	2.27 ± 1.66	1.57 ± 0.51	1.58 ± 0.46	2.20 ± 1.12	1.92 ± 0.95	1.73 ± 0.28
Geometric mean (%CV)	1.92 (74.0)	1.49 (36.5)	1.51 (35.6)	1.96 (63.5)	1.78 (44.1)	1.71 (17.3)
Minimum-maximum	0.97 - 8.42	0.83 - 2.68	0.92 - 2.37	0.85 - 4.69	1.17 - 5.30	1.23 - 2.34
AUC(tlast) (ng*h/mL)						
Arithmetic Mean ± SD	5.33 ± 2.56	24.0 ± 6.12	31.8 ± 5.10	4.68 ± 2.89	20.6 ± 6.53	33.4 ± 7.95
Geometric Mean (%CV)	4.95 (44.9)	23.2 (31.6)	31.3 (18.7)	4.15 (61.9)	19.4 (49.1)	32.5 (26.7)
Minimum-Maximum	2.26 - 15.1	12.4 - 36.0	21.2 - 41.1	1.24 - 15.5	5.44 - 35.0	21.0 - 49.7
Cl/f (L/h)						
Arithmetic mean ± SD	30.6 ± 12.5	18.6 ± 5.57	17.7 ± 3.49	46.3 ± 25.3	27.3 ± 15.1	20.9 ± 5.24
Geometric mean (%CV)	28.4 (42.1)	18.0 (26.7)	17.4 (19.7)	41.6 (49.7)	24.8 (42.9)	20.3 (24.7)
Minimum-maximum	8.42 - 73.9	12.5 - 34.9	11.9 – 24.4	12.3 - 138	14.3 - 80.6	13.8 - 32.9
Vz/f (L)						
Arithmetic mean ± SD	104 ± 94.8	42.1 ± 18.1	40.4 ± 14.5	147 ± 102	73.8 ± 48.7	51.9 ± 14.3
Geometric mean (%CV)	78.9 (80.6)	38.8 (43.2)	37.9 (39.1)	118 (81.1)	63.6 (57.6)	50.2 (26.5)
Minimum-maximum	34.5 - 354	21.3 - 92.0	19.8 - 69.2	28.4 - 444	31.0 - 237	32.8 - 94.1

AUC = area under the curve extrapolated to infinity, Cmax = maximum concentration, tmax = time to reach Cmax, t1/2 = terminal half-life,
AUC(0-tlast) = area under the curve up to the last data point, CL/f = apparent total clearance, Vz/f = apparent volume of distribution

Table 2: Second Study—sargramostim PK parameters following single SC and IV administration

Parameter	Part 1		Part 2	
	Sargramostim EDTA 6 µg/kg SC [1] N = 39 [3]	Sargramostim LY 6 µg/kg SC [1] N = 39	Sargramostim EDTA 500 µg SC [2] N = 14	Sargramostim EDTA 500 µg IV [2] N = 13
Cmax (ng/mL)				
Arithmetic mean ± SD	3.24 ± 1.12	3.15 ± 1.11	4.47 ± 0.95	16.7 ± 4.07
Geometric mean (%CV)	3.06 (36.2)	2.96 (38.0)	4.38 (20.9)	16.3 (25.5)
Minimum-maximum	1.4-6.7	1.4-5.5	3.4-6.6	9.9-23.4
AUC(tlast) (ng*h/mL)				
Arithmetic mean ± SD	20.7 ± 6.02	20.4 ± 5.86	25.0 ± 6.07	32.9 ± 6.63
Geometric mean (%CV)	19.7 (32.0)	19.5 (31.0)	24.3 (25.8)	32.3 (21.1)
Minimum-maximum	8.4-34.6	8.8-32.1	13.9-36.6	20.6-43.9
tmax (h)				
Arithmetic mean ± SD	2.17 ± 1.91	4.06 ± 1.41	0.86 ± 1.08	2.00 ± 0.00
Median	2.5	4.0	0.25	2.0
Minimum-maximum	0.25 - 8.00	2.5-7.0	0.25 -3.0	2.0-2.0
t1/2 (h)				
Arithmetic mean ± SD	1.74 ± 0.47	1.39 ± 0.36	1.92 ± 0.45	3.84 ± 4.17
Geometric mean (%CV)	1.68 (28.2)	1.35 (26.0)	1.86 (28.2)	2.24 (139)
Minimum-maximum	1.03-2.96	0.74-2.21	1.02-2.44	0.931-11.2
AUC (ng*h/mL)				
Arithmetic mean ± SD	20.7 ± 6.02	20.4 ± 5.86	25.0 ± 6.07	32.9 ± 6.63
Geometric mean (%CV)	19.8 (32.0)	19.6 (31.0)	24.3 (25.8)	32.3 (21.1)
Minimum-maximum	8.4-34.6	8.8-32.1	13.9-36.6	20.6-43.9
Cl (L/h) [4]				
Arithmetic mean ± SD	27.3 ± 8.82	25.0 ± 8.03	23.0 ± 6.26	17.2 ± 3.77
Geometric mean (%CV)	25.9 (32.9)	23.9 (32.1)	22.3 (25.8)	16.8 (21.2)
Minimum-maximum	14.1-51.7	13.8-45.4	14.8-39.0	12.2-26.3
Vz (L) [4]				
Arithmetic mean ± SD	71.0 ± 36.9	51.9 ± 26.1	64.5 ± 26.5	96.8 ± 110
Geometric mean (%CV)	62.9 (53.1)	46.3 (50.7)	59.9 (42.0)	54.4 (147)
Minimum-maximum	21.4-183	16.5-122	27.2-133	19.2-304

AUC = area under curve extrapolated to infinity, Cmax = maximum concentration, tmax = time to reach Cmax, t1/2 = terminal half-life, AUC(0-tlast) = area under curve up to last data point, CL= total clearance, CL/f = apparent total clearance (SC only), Vz= volume of distribution, Vz/f = apparent volume of distribution (SC only)

[1]: Actual dose 6.516 µg/kg based on 543 µg/mL sargramostim vial concentration

[2]: Actual dose 543 µg based on 543 µg/mL sargramostim vial concentration.

[3]: One subject excluded from PK analysis due to inadequate PK sampling.

[4]: For SC administration, CL/f and Vz/f were calculated.

6. Discussion: Rapid drug absorption after subcutaneous administration of the GM-CSF formulation with EDTA compared to the GM-CSF formulation without EDTA allows for sufficient drug concentration to be available earlier in systemic circulation, which may elicit an earlier clinical benefit.

7. The undersigned declares further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful, false statements, and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

22 MAY 2006

Catherine Scholz, Pharm.D. Date

EXHIBIT 1

Dr. Scholz's Curriculm Vitae

CATHERINE R. SCHOLZ, PHARM.D.

EXPERIENCE

Senior Clinical Research Scientist August 2004 - present
Clinical Research Scientist August 2003 - August 2004
Clinical Pharmacology
Berlex, Inc. Montville, New Jersey

- Study management and clinical trial design experience in cardiac safety, ethnic bridging, bioequivalence, and special population studies.
- Characterized the pharmacokinetics and pharmacodynamics of chemical and biological compounds in Phase I drug development
- Proficient with pharmacokinetic/pharmacodynamic modeling programs including ADAPT II, WinNonlin, and Kinetica

Clinical Pharmacology Fellow July 2001 - August 2003
The University of Texas, M.D. Anderson Cancer Center
Pharmaceutical Development Center

- Characterized the pharmacokinetics and pharmacodynamics of various anticancer agents in preclinical, Phase I, and Phase II drug development
- Proficient with pharmacokinetic/pharmacodynamic modeling programs including ADAPT II, WinNonlin, and Pharsight Trial Simulator
- Determined dose finding, toxicity, and pharmacokinetic sampling schema in murine, rat, canine and human models
- Designed pharmacology protocols for preclinical and clinical trials
- Developed analytical assays for the identification and quantification of compounds in biomatrices utilizing HPLC, GC/MS, and LC/MS/MS instrumentation

Staff Pharmacist October 2000 - June 2001
CVS Pharmacy
Northern and Central Districts, New Jersey

- Responsible for all steps in the prescription filling process including: drug utilization review, drug interaction monitoring and dispensing.
- Communicated drug information to patients and health care providers to insure safe and effective product utilization
- Supervision of pharmacy personnel
- Maintained pharmacy inventory
- Completed appropriate pharmacy paperwork, daily logs, and weekly operational data

EDUCATION

Doctor of Pharmacy May 2001
Bachelor of Science, Pharmacy with honors May 2001
Rutgers, The State University of New Jersey
College of Pharmacy
Piscataway, New Jersey

PHARMACY LICENSURE

New Jersey – RI27493

PRESENTATIONS

- Catherine Scholz, Timothy Madden, David P. Ryan, J. Paul Eder, Panos Fidias, Roberto Guerciolini, Narith Sao, Jeffrey G. Supko, and Darrell Nix. **"Pharmacokinetics of gemcitabine and the proteasome inhibitor bortezomib (formerly PS-341) in adult patients with solid malignancies"** Making a Difference in Oncology (MADONC) Conference, Phoenix, Arizona. April 2003.

- Catherine Scholz, Mary J Johansen, Robert Newman, Michael Andreeff, Marina Konopleva, and Timothy Madden. "Sensitive and specific method for the determination of CDDO methyl ester in mouse, rat, dog, monkey, and human plasma by LC-tandem mass spectrometry" American Association for Cancer Research Annual Meeting, Toronto, Canada. April 2003.

- Mary J Johansen, Catherine Scholz, Robert A Newman, Neil C Thapar, Michael Andreeff, Marina Konopleva, and Timothy Madden. **"Pharmacology and preclinical pharmacokinetics of the triterpenoid CDDO methyl ester"** American Association for Cancer Research Annual Meeting, Toronto, Canada. April 2003.

- Henry Q. Xiong, Roy Herbst, Silvana Faria, Darren Davis, Catherine Scholz, Edward Jackson, Timothy Madden, David McConkey, Marshall Hicks, Kenneth Hess, Chusilp Charnsangavel, and James Abbruzzese. **"A phase I surrogate endpoint trial of SU6668 in patients with solid tumors"** American Association for Cancer Research Annual Meeting, Toronto, Canada. April 2003.

- **"Farnesyl Transferase Inhibitors: Targeting Ras and beyond..."** Division of Pharmacy Grand Rounds, University of Texas M.D. Anderson Cancer Center, Houston, Texas. April 2003.

- **"Farnesyl Protein Transferase Inhibitors: Is Ras the Real Target?"** Pharmaceutical Development Center, University of Texas M.D. Anderson Cancer Center, Houston, Texas. November 2002.

- **"Angiogenesis and the Role of SU6668"** Pharmaceutical Development Center, University of Texas M.D. Anderson Cancer Center, Houston, Texas. November 2001.

- **"Rapacuronium: An Alternative to Succinylcholine for Rapid Tracheal Intubation?"** Fall 2000 Clinical Seminar Series, Rutgers University: College of Pharmacy, Piscataway, New Jersey. October 2000.

- **"New Therapeutic Approaches: Selective Serotonin Reuptake Inhibitors and Atypical Antipsychotics."** Sherlin Associates, Inc., West Orange, New Jersey. October 2000.

- **"Buprenorphine and Methadone: A review of heroin detoxification."** Catholic Communities Service, patient inservice, Newark, New Jersey. October 2000.

- **"Drospirenone: A Novel Progesterone."** Ortho McNeil Pharmaceutical, Inc. Medical Affairs, Raritan, New Jersey. September 2000.

- **"Hormone replacement therapy and peripheral arterial disease: the Rotterdam study."** Ortho McNeil Pharmaceutical, Inc., Medical Affairs, Raritan, New Jersey. September 2000.

CLINICAL CLERKSHIPS

Drug Information February - March 2001
Robert Wood Johnson University Hospital
New Brunswick, New Jersey
Preceptor: Lois Jessen, M.S., Pharm.D.
Evelyn Hermes-DeSantis, Pharm.D., BCPS

Emergency Medicine January - February 2001
Robert Wood Johnson University Hospital
New Brunswick, New Jersey
Preceptor: Kevin Rynn, Pharm.D., ABAT

Oncology November - December 2000
Hackensack University Medical Center
Hackensack, New Jersey
Preceptor: Matthew Cimino, Pharm.D.

Consulting Pharmacy October - November 2000
Sherlin Associates, Inc.
West Orange, New Jersey
Preceptor: Barry Cook, R.Ph., CCP

Pediatrics/Critical Care August - September 2000
Robert Wood Johnson University Hospital
New Brunswick, New Jersey
Preceptor: Marc Sturgill, Pharm.D.

Nephrology/Ambulatory Care May - June 2000
Robert Wood Johnson University Hospital

New Brunswick, New Jersey
Preceptor: Edward Foote, Pharm.D., BCPS

HONORS

▪ Bachelor of Science, Pharmacy with Honors	May 2001
▪ Excellence in Clinical Information, Facts and Comparisons	May 2001
▪ Dean's List	1996 - 1999
▪ Rutgers Alumni Association Award	1997 – 1998

PROFESSIONAL ORGANIZATIONS

▪ American Association of Pharmaceutical Scientists	2004 - present
▪ Alpha Zeta Omega	1995 - present
President	1998
Excheque	1997 – 1998
Recording Signare	1996 – 1997
▪ Rutgers University, College of Pharmacy Big Brother/Big Sister	1996 – 1999
▪ Pharmacy Governing Council	1995 - 1999

EXHIBIT 2

Mean (SD) sargramostim concentration (ng/mL) v. Time (h) after subcutaneous administration of the sargramostim formulation without EDTA (LYO) and with EDTA (EDTA)

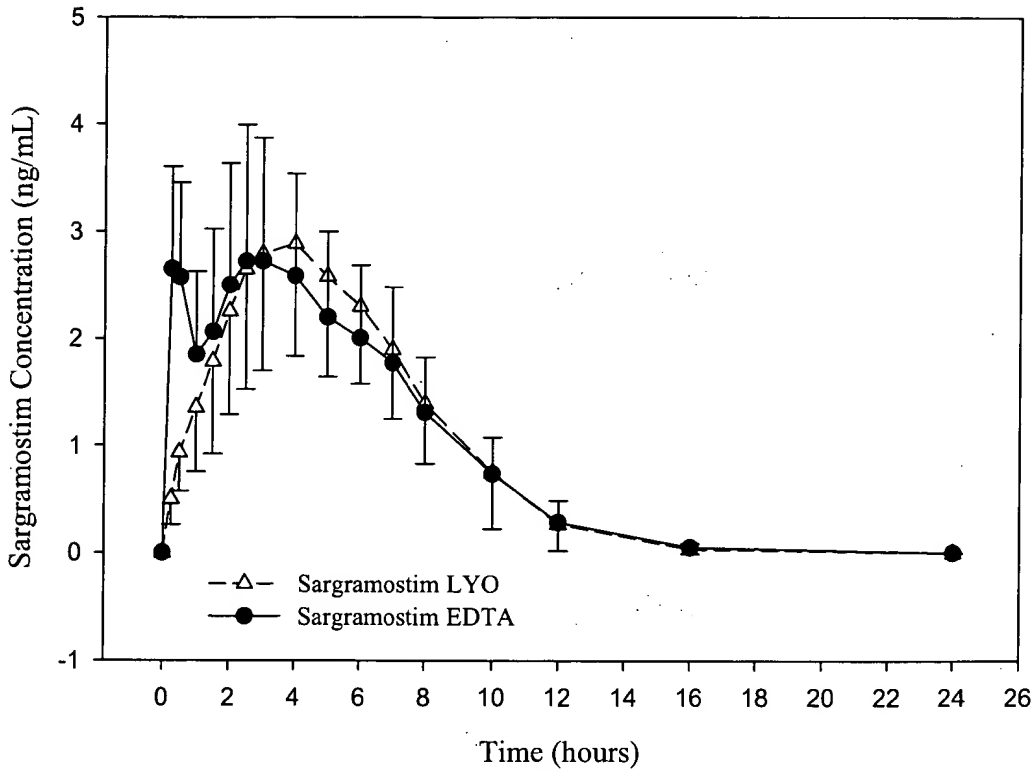


EXHIBIT 3

Mean sargramostim concentration (ng/mL) v. Time (h) after subcutaneous administration of the sargramostim formulation without EDTA (LYO) and with EDTA (EDTA) [semi-logarithmic scale]

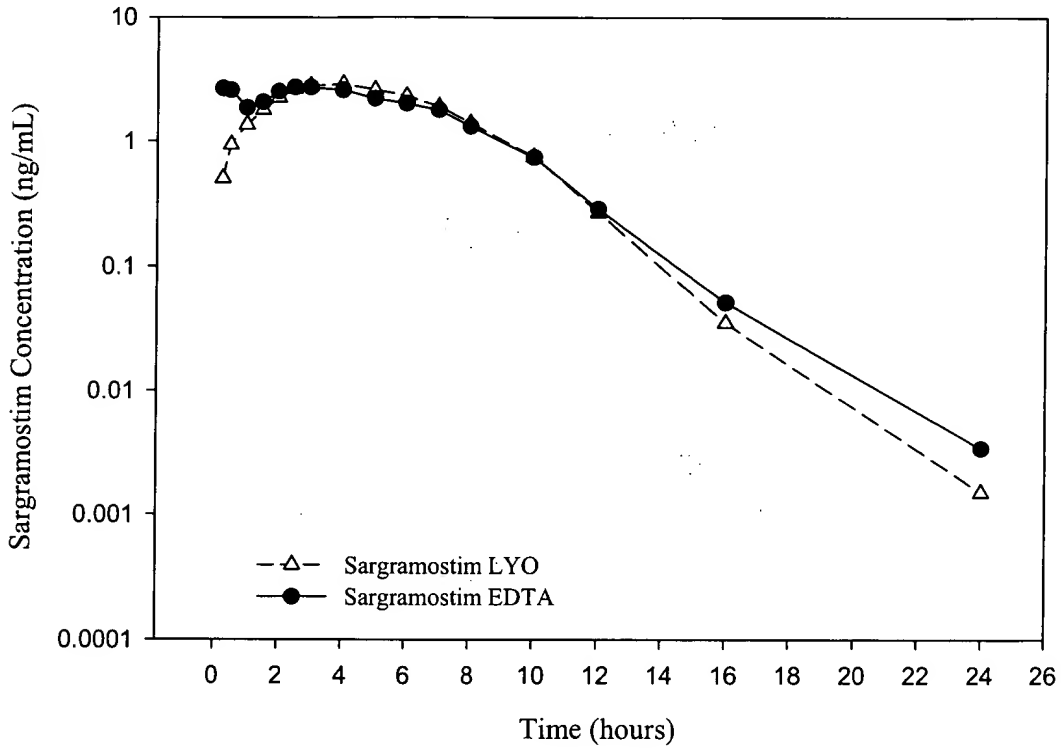


EXHIBIT 4

Mean sargramostim concentration (ng/mL) v. Time (h) after subcutaneous administration of the sargramostim formulation with EDTA

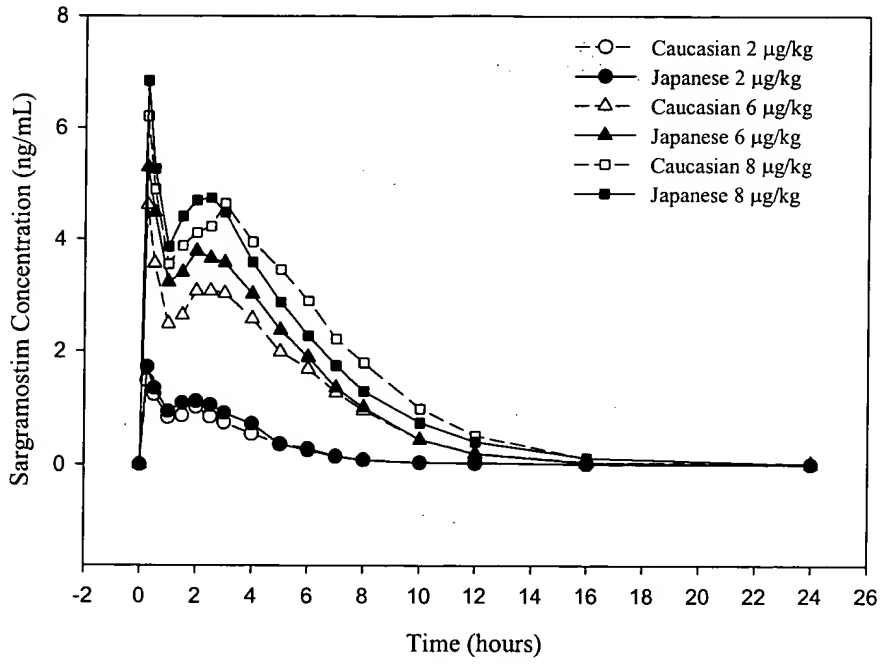


EXHIBIT 5

Mean sargramostim concentration (ng/mL) v. Time (h) after subcutaneous administration of the sargramostim formulation with EDTA [semi-logarithmic scale]

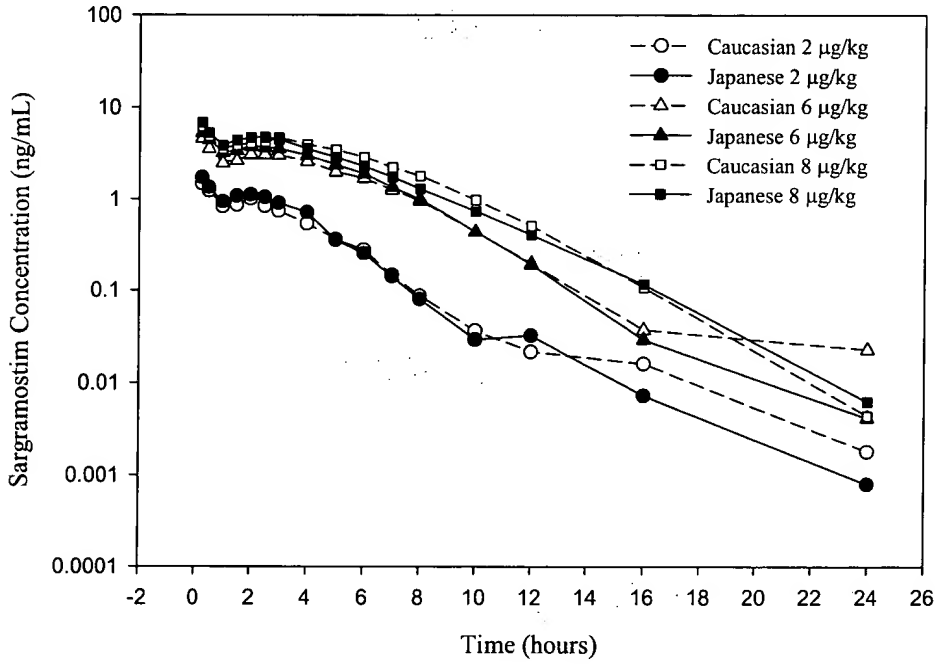
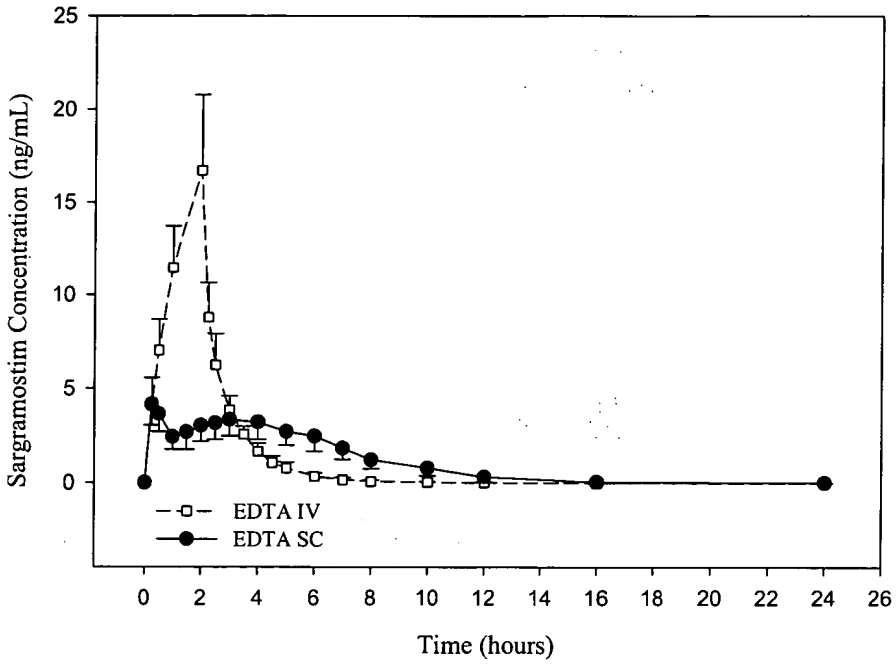


EXHIBIT 6

Mean sargramostim concentration (ng/mL) v. Time (h) after subcutaneous administration and intravenous administration (2-hour) of the sargramostim formulation with EDTA



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